UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,667	07/27/2006	Thomas Lampe	584212002600	8586

25225 7590 02/05/2008

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
02/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,667	LAMPE ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Current Status of 10/522667

1. Claims 1-15, 17, 19, and 20 are pending in the instant application and are being examined in the current office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-15, 17, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the parent compounds and their salts, does not reasonably provide enablement for solvates or solvates of salts of the claimed compound. While providing enablement for treatment of bacterial infections, the specification does not enable the use of the instant compounds to prophylax (prevent) or "control" bacterial infections broadly . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make solvates or salts of solvates or to use the compounds to prophylax or control bacterial infections to level of preventing bacterial infections commensurate in scope with these claims. Vippagunta et al. (*Advanced Drug Delivery Reviews*, **2001**, *48*, 3-26) show that solvate formation is unpredictable because each compound has a unique chemical nature (page 18, section 3.4). Applicants are not enabled for the prevention or control of bacterial infections broadly. Syphilis, one bacterial infection, is not preventable ("Syphilis facts", http://www.dhpe.org/infect/syphilis.html, accessed January 10, 2008). The instant disclosure does not enable claim 19, drawn to the treatment and prophylaxis of bacterial infection because these alternative methods require therapeutic treatment directed to divergent patient

populations. The population to be treated would encompass individuals already infected with bacteria, whereas the population intended to benefit from prophylaxis and control of bacterial infection are interpreted to encompass patients who would not have a bacterial infection. Requisite treatment of said patient populations requires procedures which involve very different parameters, concerns and modalities for therapy. The wording of the claims as they currently stand implies the same population is being treated for bacterial infections and prevented from having a bacterial illness coincidently.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to biphenomycin analogs that are being used to treat, prophylax or control bacterial infections broadly. The claims do not specify the type of bacteria to be treated and are interpreted broadly to intend the treatment, control or prophylaxis of all types of bacteria.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Vippagunta teaches that the current state of the art in the formation of solvates is unpredictable. There are bacteria that cannot be prevented such as syphilis and in the

absence of proof to the contrary, the skilled artisan would indeed question the objective truth that bacteria can be controlled or prevented as applicants have broadly asserted in the instant claims.

(5) The relative skill of those in the art:

One of ordinary skill in the art is familiar with the synthetic techniques shown in the specification and skilled in the treatment or prevention of bacterial infections in patient populations.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification does not provide support or sufficient guidance for the preparation of solvates or solvates of salts of the instantly claimed compounds. The specification has provided guidance for the treatment of gram-positive and gram-negative bacteria with compounds of claim 1. However the specification does not provide guidance that supports methodological procedures that encompass prophylaxis of bacterial infection or control of bacterial infection to the degree of prevention.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regard to the high degree of unpredictability in the art of solvate preparation and the art of bacterial control and prophylaxis in view of the lack of guidance provided in the specification to address these deficiencies, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3, 6-15, 17, 19, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. What groups are specifically referred to in variable R^1 when it is a "carbonyl linked amino acid residue"? The specification gives a generic definition (page 10, line 30 to page 11, line 3) of this group, but the amino acid can be any amino acid, natural or unnatural. For variable R^3, what groups are represented by "hydroxy linked amino acid residue"? The specification gives a generic definition (page 11, lines 5-10), but the hydroxyl group can be attached to any point of any amino acid. For variable R^5, what specific chemical moieties are represented by "side chain group of an amino acid"? This group is broadly defined in the specification (page 10, lines 13-17), but this definition provides for any side chain of an amino acid, including glycine.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 2, 9-12, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Carlstrom et al. (*Journal of the Chemical Society, Chemical Communications*, **1991**, 1216-17). Carlstrom et al. teach compound 1(page 1216), which anticipates claims 1,2, 9-12, and 20 because variables R^5, R^7, and R^8 are methyl (alkyl), and NR^1R^2 is NH-BOC (*t*-butoxycarbonyl)(an alkoxycarbonyl group). Variables R^3 and $R^{3'}$ are an aminocarbonyl-substituted alkyl group and H respectively. Claim 20 is anticipated because the introduction

teaches that biphenomycin analogs of the reference are effective against *Streptomyces griseorubinosus*, a gram-positive bacterium.

8. Claims 1-3 and 9-15 rejected under 35 U.S.C. 102(b) as being anticpated by Sandstrom (*Chirality*, **1995**, *7*, 181-192). Sandstrom reports compound 3c (page 187) which anticipates compounds of claims 1-2 and 9-15 because variables on the biphenomycin core of the reference teach R^5, R^7, and R^8 are each methyl, R^3 is amino-substituted alkyl, and $R^{3'}$ is H.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1-3, 13-14, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlstrom et al. (same reference as 102(b) rejection). Compound 1 teaches the methyl group in variables R7 and R8. H vs. Me is deemed a patentable advance evidence of superior, unexpected results (*In re Wood*, 199 USPQ 137). As mentioned previously, these compounds are being used against gram-positive bacteria.

12. Claims 1-14, 17, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ezaki et al. (*Journal of Antibiotics*, **1985**, *38(11)*, 1453-61). Ezaki et al. teach biphenomycin B, which renders the claims obvious because biphenomycin B is used for the treatment of bacterial infections as set firth in the instant application. It is used to treat bacteria, specifically *S. aureus* (table 6, page 1460). Biphenomycin B renders the claims obvious because the biphenomycin core of the reference is modified wherein variables R^7 and R^8 are H, NR^1R^2 is NH_2, and R3 is 2-hydroxy-3-amino-propyl. The biphenomycin B of the instant invention and of the reference differ at the variable R^5. Variable R^5 cannot be methyl. However, this paper shows that when R^5 is H, this compound is still effective against bacteria and other microorganisms. Compositions of biphenomycin B with different agars (which are pharmaceutically acceptable excipients) are taught on page 1460.

13. Claims 1-3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sandstrom in view of Carlstrom et al. Compound 3c (page 187) only differs from a compound of claim 3 because variable R^8 is methyl. However, H vs. Me is no deemed a patentable advance absent superior, unexpected results. Carlstrom teaches that biphenomycin analogs can treat gram-positive bacteria. Since compound 3c can be considered a biphenomycin analog because it has the same skeleton as biphenomycin A or B, compound 3c can be considered a biphenomycin analog. Therefore, motivation for making this compound exists. One of ordinary skill in the art could test this compound's ability to inhibit *S. aureus* or *E. coli*, for example.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1, 17, 19, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 22-25, and 27 of copending Application No. 11/453375. Although the conflicting claims are not identical, they are not patentably distinct from each other because example 28J (page 88) of the specification is an obvious variant of claimed compounds in claim 1 in copending application 11/453375. In compound 28J, variable R^5 is methyl (claim 1 of 11/453375 allows for H and amino). The compounds in 11/453375 are being used for the same purpose in the instant application. In addition, in view of the teachings of *Ex Parte Weston* (121 USPQ 428), H vs. methyl is not deemed to be patentably distinct without evidence of superior, unexpected results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

16. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Patent Examiner
Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner
Art Unit 1624